REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 1-9 are pending in the application and stand rejected.

Claims 1 and 9 have been amended.

Claim 1 has been amended to more clearly describe the claimed subject matter. Support for the amendments to claim 1 can be found throughout the original disclosure, particularly in the claims as originally filed.

Claim 9 has been amended to depend from claim 5 for clearer antecedent basis for the term "dermatitis."

The Abstract has been replaced with a new Abstract. The Abstract has been corrected to address the formal objections raised in the Office Action.

No prohibited new matter has been introduced by way of the above amendments. Applicants reserve the right to file a continuation or divisional application on subject matter canceled by way of this Amendment.

Formal Objections

The Abstract has been objected to because of punctuation errors. By the present amendment, the Abstract is amended to correct the cited punctuation errors. Withdrawal of the objection is requested.

Claim 9 has been objected to as allegedly lacking antecedent basis for the term "dermatitis." Claim 9 has been amended to depend from claim 5, in which antecedent basis for "dermatitis" may be found. Withdrawal of the objection is requested.

Rejections under 35 U.S.C. § 112

Claims 1-9 stand rejected under 35 U.S.C. § 112 as allegedly containing subject matter that fails to satisfy the written description requirement. The rejection is respectfully traversed.

The Office has alleged that "the skilled artisan [could not] envision the detailed chemical structure of the encompassed polypeptides which include variants having as little as 70% sequence identity with SEQ ID NO:1 and fragments having as few as 2 amino acids in common with SEQ ID NO:1." Applicants respectfully point out that the genus of polypeptides having 70% or greater identity to a sequence set forth in SEQ ID NO:1 is a mathematically unambiguous genus. Thus, every member of the genus may be envisioned.

Without acceding to the allegations of the rejection, but simply in order to better describe the claimed subject matter, claim 1 has been amended to replace an "an" with a "the" and to cancel the recitation of "a polypeptide having at least 70% sequence homology."

Claims 1-9 as currently presented clearly satisfy the written description requirement. Accordingly, withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 112

Claims 1-9 stand rejected under 35 U.S.C. § 112 as allegedly containing subject matter that is not supported by an enabling disclosure in the specification. The rejection is respectfully traversed.

The Office has alleged that "the specification, while being enabling for a method of treating wounds by administering the polypeptide of SEQ ID NO:1, does not reasonably provide enablement for methods of treating wounds comprising administering polypeptides with 'at least 70% sequence homology' of SEQ ID NO:1 or for fragments of the polypeptide of SEQ ID NO:1."

The burden is upon the Office to set forth sufficient reasons to show that one of ordinary skill in the art would be unable to make and use the invention commensurate in scope with the claims. The Office has failed to do so. The Office provides a single unrelated example to imply that the art is unpredictable. Such a single unrelated example is insufficient to prove that the art in general or the claimed invention in particular is so unpredictable that one of skill in the art could not make and use the claimed invention without undue experimentation. On the other hand, the application provides guidance with respect to the sort of substitutions that may be used to obtain functional equivalents, for example in the paragraph bridging pages 6-7 of the substitute specification filed November 15, 2004.

Without acceding to the allegations of the rejection, but simply in order to expedite prosecution of subject matter that the Office has acknowledged is enabled, claim 1 has been amended to replace an "an" with a "the" and to cancel the recitation of "a polypeptide having at least 70% sequence homology."

Claims 1-9 as currently presented clearly satisfy the enablement requirement. Accordingly, withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 103

Claim 1 stands rejected under 35 U.S.C. § 103 as allegedly unpatentable over Kim et al. (WO 0195927) in view of Gallucci et al. (FASEB J, 14:2525-31, 2000). The Office has

alleged that Kim et al. teaches the polypeptide p43 having an identical sequence as SEQ ID NO:1. The Office correctly acknowledges that Kim et al. do not teach a method of stimulating wound healing by administering the polypeptide of SEQ ID NO:1.

The Office alleges that Gallucci et al. teach that IL-6, an inflammatory cytokine, promotes wound healing in IL-6 deficient mice. The Office further alleges that it would have been obvious to use the polypeptide of SEQ ID NO:1, which is a pro-inflammatory cytokine taught by Kim et al. for treating wounds, because Gallucci et al. suggest that IL-6 is associated with wound healing.

However, the cited art fails to establish a proper prima facie case of obviousness. To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. M.P.E.P. § 2143.

It is impermissible to first ascertain factually what applicants did and then view the prior art in such a manner as to select from the random facts of that art only those which may be modified and then utilized to reconstruct applicant's invention from such prior art. *Interconnect Planning Corp. v. Feil*, 150 U.S.P.Q. 54, 57 (C.C.P.A 1966); *In re Shuman*, 774 F.2d 1132, 1142-3, 227 U.S.P.Q. 543, 550 (Fed. Cir. 1985). Here, the Office is selectively interpreting the cited documents to fit the art to Applicant's invention. However, upon consideration of the documents as a whole and in the absence of hindsight, the cited documents would not suggest the presently claimed invention. The Office is using hindsight

to stretch the teachings of Galluci et al. to fit its conclusion. This is impermissible and the rejection should be withdrawn.

According to Gallucci, et al(FASEB J. 14:2525-2531, 2000), IL-6 KO mice displayed decreased inflammation and granulation tissue formation, and showed incomplete re-epithelialization. *See*, Gallucci et al. at figure 1. Moreover, the IL-6 KO mice were administered rmIL-6 before wounding. Treatment with rmIL-6 allowed wound healing to occur at a similar rate to that in wild-type mice. *See*, Gallucci et al. at lower left column of page 2528 and figure 4. That is to say, Gallucci, et al teach that transfer of rmIL-6 into IL-6 KO mice produced only a reversal of the healing deficiency of IL-6 KO mice. Gallucci et al. does not teach or suggest that IL-6 actually stimulates wound healing, particularly in an IL-6 normal background.

The results reported by Gallucci, et al. suggest only that IL-6 is a cytokine associated with wound healing to the extent that its absence causes a deficiency in healing. However, because there is no experimental data to show whether the wound healing would be promoted in a case where wounded wild-type mice are treated with IL-6, it is not clear that IL-6 promotes wound healing. Gallucci, et al also suggest that the IL-6 role in wound healing is indirect. See, Galluci et al. at the lower right column of page 2528. However, a person of ordinary skill in the art would not know from reading Galluci et al. whether such indirect support could promote wound healing in a method of treatment.

Given the limited teaching of Gallucci et al., the proposed combination provides neither a suggestion to combine the cited references or a reasonable expectation of success in doing so. At best Galluci et al. constitutes a suggestion to conduct further research into the role of IL-6, and cannot even be construed as an invitation to conduct research trying any pro-inflammatory cytokine. Moreover, even if it were obvious to undertake research to try

any cytokine, that would not constitute a prima facie case of obviousness for the claimed invention. The Federal Circuit has consistently held that "obvious to try" is not to be equated with obviousness under 35 U.S.C. § 103. *See, e.g., Gillette Co. v. S.C. Johnson & Son Inc.,* 16 U.S.P.Q.2d 1923, 1928, 919 F.2d 720 (Fed. Cir. 1990) (citing *In re O'Farrell,* 853 F.2d 894, 903-04, 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1380, 231 U.S.P.Q. 81, 91 (Fed. Cir. 1986); and *Jones v. Hardy*, 727 F.2d 1524, 1530, 220 U.S.P.Q. 1021, 1026 (Fed. Cir. 1984)).

Compared with the teachings of the cited documents, in the present invention, in order to identify the stimulating effect of p43 on wound healing, p43 treatment in wounded wild-type mice was compared with no treatment in examples. As a result, it was shown that the wound area was rapidly decreased in the p43 treated wild-type mice. *See*, Specification at example 4 and figure 4. Additionally, p43 treatment in wounded wild-type mice displayed increase of granulation tissue and rapid re-epithelialization by increase of advancing epithelial layer. *See*, Specification at figure 5.

Moreover, any apparent relevance of Gallucci et al. is negated, because IL-6 is not related to the effect of p43. In the present invention, to determine the effect of p43 on the proliferation of foreskin fibroblasts, the foreskin fibroblasts were cultivated in the presence of the different amounts of p43 (1, 10 and 100 ng/ml) for 48 hours. *See*, Specification at Example 4.4.1. As a result, the proliferation of fibroblasts was significantly increased in dose-dependent manner by p43. *See*, Specification at figure 7. Through the example 4.4.1, it is clear that the effect of p43 on stimulation of wound healing is not related to IL-6.

Moreover, the assertion of the Office that it would be obvious to combine the cited references, because IL-6 is a pro-inflammatory cytokine is in error, because it is clear that

pro-inflammatory cytokines do not always stimulate wound healing. This is shown, for example, by experimental data. (See, Exhibit A, attached.)

It is known that p43 is a precursor of EMAP II, and EMAP II has cytokine activity. *See*, Kim, et al. WO 0195927 at page 2, paragraph 2. However, according to the experimental data, p43 has both cytokine activity and the effect on stimulation of wound healing and EMAP II (C-terminal domain of p43) has cytokine activity and no effect on stimulation of wound healing. Although EMAP II has the C-terminal domain of p43 and both EMAP II and p43 are pro-inflammatory cytokine, their activities for stimulation of wound healing are different.

Therefore, it would not be obvious to one skilled in the art, nor would there be a reasonable expectation of success in trying p43 in a method of wound treatment even if Gallucci, et al or any other documents were found to teach that IL-6 or any other pro-inflammatory cytokine participates in wound healing. However, as discussed above, Gallucci, et al does not even present any experimental data or descriptions that IL-6 directly stimulates wound healing.

For at least the foregoing reasons, the Office has failed to set forth a prima facie case of obviousness. Accordingly, withdrawal of the rejection is respectfully requested.

Claims 2-9 have been rejected under 35 U.S.C. § 103 as allegedly unpatentable over Kim et al. (WO 0195927) in view of Gallucci et al. (FASEB J, 14:2525-31, 2000) and further in view of Bennett et al. (Am J. Surg., 165:728-37, 1993). Kim et al. and Gallucci et al. are discussed above. Bennett et al. is apparently cited for suggesting that various growth factors may be used in a method to promote healing of epidermal injuries. The Office alleges that it

would be obvious to treat any type of wound with any combination of any compounds known to promote healing of epidermal injuries.

However, Bennett et al. does not cure the deficiencies of Kim et al. and Gallucci et al. Bennett et al. provides no further teaching that would tend to provide a suggestion to combine Kim et al. with Gallucci et al., or a reasonable expectation of success that the proposed combination would be successful. In the absence of any such teaching or reasonable expectation, a person of ordinary skill would have no reason to think that p43 should be combined with any of the compounds taught by Bennett.

For at least the foregoing reasons, the proposed combination of Bennett et al. with Kim et al. and Gallucci et al. does not constitute a prima facie case of obviousness. Accordingly, withdrawal of the rejection is respectfully requested.

Claims 1, 4 and 7 have been rejected under 35 U.S.C. § 103 as allegedly unpatentable over Kim et al. (WO 0195927) in view of Gallucci et al. (FASEB J, 14:2525-31, 2000) and further in view of Goddard et al., U.S. Patent No. 6,916,648. Kim et al. and Gallucci et al. are discussed above. Goddard et al. is apparently cited for suggesting that VEGF is useful for treating diabetic ulcers and vascular injuries. The Office alleges that it would be obvious to treat any type of wound with any combination of any compounds known to promote wound healing.

However, Goddard et al. does not cure the deficiencies of Kim et al. and Gallucci et al. Goddard et al. provides no further teaching that would tend to provide a suggestion to combine Kim et al. with Gallucci et al., or a reasonable expectation of success that the proposed combination would be successful. In the absence of any such teaching or

reasonable expectation of success, a person of ordinary skill would have no reason to think that p43 should be combined with a treatment with VEGF taught by Goddard et al.

For at least the foregoing reasons, the proposed combination of Goddard et al. with Kim et al. and Gallucci et al. does not constitute a prima facie case of obviousness. Accordingly, withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL PC

Date: December 27, 2005

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